

ORIGINAL ARTICLE**Undiagnosed Diabetes Mellitus and Associated Factors among Psychiatric Patients Receiving Antipsychotic Drugs at The University of Gondar Hospital, Northwest Ethiopia**

Daniel Asmelash^{1*}, Wondale Getnet¹, Belete Biadgo², Sintayehu Ambachew², Tadele Melak², Lemmesa Melese², Shiwaneh Damite², Habtamu Wondifraw Baynes², Molla Abebe¹

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Affiliation and Correspondence:

¹Department of Clinical Chemistry, School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia

²University of Gondar Hospital Laboratory, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia

*Email: daniel.asmelash111@gmail.com

ABSTRACT

BACKGROUND: Undiagnosed diabetes mellitus cases are at higher risk for diabetic related complications. In low-income African countries, patients with undiagnosed diabetes mellitus account for 75% of diabetes cases. Psychiatric disorders have a greater impact on the global burden of diseases and disability associated with chronic diseases like diabetes mellitus and cardiovascular diseases.

METHODS: Institution based cross-sectional study was conducted at the University of Gondar Hospital from February to April 2016. A total of 205 psychiatric patients aged above 15 years that were taking antipsychotic were included by the simple random sampling method. Fasting blood glucose, triglycerides and cholesterol level were determined from venous blood samples to evaluate diabetes mellitus based on WHO criteria.

RESULTS: Among 205 psychiatric patients taking antipsychotics, 15(7.3%) had undiagnosed diabetes mellitus. Duration of antipsychotic treatment and sex had a statistically significant association with the prevalence of undiagnosed diabetes mellitus. As the duration of antipsychotic drug treatment increased by one year, the risk of having a diabetes mellitus increase by 1.47 times (AOR: 1.47 CI: 1.021-2.125).

CONCLUSION: The prevalence of undiagnosed diabetes mellitus among psychiatry patients taking antipsychotics was higher than the estimated diabetes national prevalence of Ethiopia. Screening of diabetes mellitus in particular, patients having a longer duration of antipsychotic treatment is mandatory to bring more undiagnosed cases for medical attention.

KEYWORDS: Diabetes mellitus, Psychiatric disorder, Antipsychotic

INTRODUCTION

Diabetes mellitus (DM) is a complex metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action or both. There are four types of diabetes mellitus (DM), classified as type 1 diabetes mellitus, type 2 diabetes mellitus (T2DM), gestational diabetes and other types of DM (1).

In 2013, 382 million people had DM; this number is expected to rise to 592 million by 2035. Most people with the DM live in low and middle-income countries (2). Ethiopia ranked among the ten top countries in Africa with a higher prevalence of DM. According to International diabetic federation (IDF) estimated national diabetes prevalence was 4.36% in 2013 (3).

About 75% of the DM patients are estimated to be undiagnosed in low-income African countries (4). The undiagnosed DM cases, they remain untreated and they are one of the reasons for a poor glycemic control level of patients. This will cause diabetic complications, such as heart, kidney, and eye diseases, lower limb amputations and mental disorders (3, 5).

Psychiatric disorder or mental disorder is a clinically significant behavioral or psychological syndrome or pattern that occurs in an individual and associated with present distress or disability (6). In 2010, mental, neurological and substance use disorders accounted for 10.4%, 2.3% and, 28.5% of global disability life years, yet remain the lowest on the agenda of policy-makers, particularly in developing countries (7, 8). Study done in Ethiopia shows, the major psychiatric disorders are schizophrenia (56.1%) followed by bipolar disorder (20.6%) and major depressive disorder (MDD) (11.4%) (8).

People with mental illness such as schizophrenia, depression or bipolar disorder have worse physical health and reduced life expectancy compared to the general population. This excess mortality is due to the fact that people with mental disorder are more likely to be overweight, and to have DM, hypertension and dyslipidemia (9, 10).

Despite the increased risk of DM and cardiovascular disease (CVD), many patients with mental disorder have limited access to general health care with less opportunity for CVD and DM risk screening and prevention than would be expected in non-psychiatric population (11, 12).

DM is highly prevalent in people with psychotic disorders, including schizophrenia and schizoaffective disorders. The exact prevalence is difficult to estimate since DM is often under-diagnosed in people with psychiatric disorders. The association between DM and psychosis is complex and multifactorial. Antipsychotic medication, poor lifestyle and genetic loading increase DM risk (12).

In addition, chronic stress is a risk factor in the incidence of DM and worsens metabolic control, which leads to diabetes-related complication. Patients with psychiatry disorder shows over-activation of both the hypothalamic–pituitary–adrenal medullary axes. These endocrine systems respond to stress by an increase in the production of diabetogenic hormones cortisol and adrenaline. It is proposed that both hormones can raise blood sugar and play a part in insulin resistance and the onset of DM (13).

Research findings from different studies indicated that the prevalence of DM in psychiatric patients was higher than the one in the general population. Therefore, this study will provide information about the magnitude of undiagnosed DM in psychiatry patients taking antipsychotics since no sufficient studies have been done in Ethiopia.

METHODS

Study area, study design, and study participants:

An institution based cross-sectional study was carried out from February–April 2016 at the University of Gondar Hospital Psychiatry Clinic, which is found in Gondar Town. All psychiatric patients aged above 15 years, receiving antipsychotic drugs and voluntary to give informed consent were included.

Sample size and sampling technique: A total of 205 individuals were enrolled in the study. Psychiatric patients aged ≥ 15 years with a diagnosis of the major psychiatric problem were included. The simple random sampling technique was used to recruit study participants, who has been following antipsychotic treatment during the study period.

Data collection and laboratory methods: Data were collected by pretested and semi-structured Amharic version questionnaire using interview technique. During the data collection, patients who were taking antipsychotic drugs were interviewed by the enumerators using the questionnaire.

At every data collection spot, sufficient explanation about the aim of the research was given to the patients or caretakers of psychiatry patients. After informed consent was obtained, participants were interviewed face-to-face on the first visit, and blood samples were collected if they were in the fasting state. However, patients in the non-fasting state were instructed to be on overnight fasting eight up to ten hours. Then, three ml of blood sample was collected in a plain tube and centrifuged at 3000 RPM for 10 minutes, and serum was separated. The samples were analyzed within two hours using automated clinical chemistry analyzer (A25 BIOSYSTEM). In addition to the fasting plasma glucose (FPG), the laboratory testing included the levels of total blood cholesterol (TCHO) and triglycerides (TG). Based on the laboratory FBG result, diabetes mellitus was defined as FPG of ≥ 7.0 mmol/l (126 mg/dl).

Quality assurance: Pre-test was done to check clarity, acceptability and consistency of the structured questionnaire. The reliability of the laboratory findings was assured by implementing quality control measures during the whole process of the laboratory works (pre-analytical, analytical and post-analytical quality control steps were followed). All materials, equipment and procedures were adequately controlled. A control was run to check the functionality of clinical chemistry automation, which was used for conducting laboratory analysis.

Data processing and analysis: All patient data were registered in laboratory worksheet during the study period. Then, the data were cleaned, edited, checked for completeness and were entered to EPI info version 3.5.3 and transferred to the Statistical Package for Social Sciences (SPSS) statistical software version 20 for analysis.

The binary logistic regression model was used to examine the factors associated with undiagnosed DM among study participants. Variables with $p < 0.2$ in the bivariate analysis were considered for multivariate analysis. Then, study findings were explained in words and tables. Finally, from a multivariate logistic regression model, variables with $P\text{-value} < 0.05$ were taken as statistically significant.

Ethical approval and consent to participate: Ethical clearance was obtained from the Ethical Review Board of the School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar. Moreover, a letter of support was secured from administrators of the University of Gondar Hospital. Following an explanation of the purpose and the possible risks of the study, written consent was obtained from all study subjects, which assured that participation was on a voluntary basis. Participants with positive results for diabetes mellitus were referred for treatment to the Diabetic Clinic within the Hospital. The collected data were kept confidential.

RESULTS

Socio-demographic characteristics of the study participants: A total of 205 psychiatric patients taking antipsychotics were included in the study. Out of all the study participants, 108 (52.7%) were females. The mean age of the study participants was 33.73 ± 11.46 (range: 15 to 81 years), and the majority (60.5%) of the study participants were urban inhabitants (Table 1).

of antipsychotic drug treatment was 2.62 ± 1.8 years. The mean duration of antipsychotic treatment for patients with an undiagnosed DM was Mean \pm SD of 4.4 ± 1.53 years. (Table 2).

Table 1: Socio-demographic characteristics of psychiatric patients receiving antipsychotic drugs at the University of Gondar Hospital, northwest Ethiopia, 2016 (n=205).

Variable	Number	%
Sex		
Male	97	47.3
Female	108	52.7
Age		
<25	54	26.3
25-34	74	36.1
35-45	42	20.5
>45	35	17.1
Marital Status		
Single	107	52.2
Married	68	33.1
Separated/divorced	29	14.1
Widowed	1	0.5
Educational Status		
Illiterate	101	49.3
Read and write	39	19.0
Primary & secondary School	37	18
College and Above	28	13.7
Religion		
Orthodox	171	83.4
Muslim	30	14.6
Others	4	2
Residence		
Rural	81	39.5
Urban	124	60.5

Behavioral characteristics of the study participants: The majority of the participants were schizophrenia patients, 106 (51.7%), followed by MDD, 68 (33.2%), and Bipolar disorder, 31 (15.1%). Almost all of the study participants, 203 (99%), had no family history of DM. Nine out of 15 (60%) DM cases were schizophrenia patients, six out of 15 (40%) undiagnosed DM cases were MDD patients and there was no case of undiagnosed DM in Bipolar patients. The mean duration of antipsychotic drug treatment was 2.62 ± 1.8 years. The mean duration of antipsychotic treatment for patients

with undiagnosed DM was 4.4 ± 1.53 years. (Table 2).

Prevalence of undiagnosed diabetes mellitus: According to the ADA criteria, the prevalence of undiagnosed DM was 7.3% (CI: 3.74 - 10.86). Among participants with undiagnosed DM, the prevalence of undiagnosed DM was more prevalent in females than males (5.9% vs. 1.5%) (P-value=0.028). The prevalence of undiagnosed DM increased across four age groups: 0%, 1.5%, 2.4% and 3.4% among participants aged < 25, 25-34, 35-45 and above 45 years respectively (Table 3).

Table 2: Prevalence of undiagnosed diabetes mellitus by behavioral characteristics, clinical and anthropometric measurements of study participants at University of Gondar Hospital, northwest Ethiopia, 2016

Variable	Category	Total N (%)	UDM	
			Yes N (%)	No N (%)
Smoking status	Non smoker	191(93.2)	14(6.8)	177(86.3)
	Current Smoker	12(5.9)	1(0.5)	11(5.4)
	Ex-smoker	29(1)	0(0)	2(1)
Physical activity	Light	61(29.8)	15(7.3)	46(22.4)
	Moderate	105(51.2)	0(0)	105(51.2)
	Vigorous	39(19)	0(0)	39(19)
Blood Pressure	Non hypertensive	196(95.6)	13(6.3)	183(89.3)
	Pre hypertensive	7(3.4)	1(0.5)	6(2.9)
	Hypertensive	2(1)	1(0.5)	1(0.5)
BMI	Underweight	19(9.3)	1(0.5)	18(8.8)
	Normal	137(66.8)	1(0.5)	136(66.7)
	Overweight	38(18.5)	11(5.4)	27 (13.2)
	Obese	10(4.9)	2(1)	8(3.9)
Family History of DM	Yes	2(1)	0(0)	2(1)
	No	203(99)	15(7.3)	188(91.7)
Type of disorder	Schizophrenia	106(51.7)	9(4.4)	97(47.3)
	MDD with Psychotic	68(33.2)	6(2.9)	62(30.2)
	Bipolar with Psychotic	31(15.1)	0(0)	31(15.1)
Antipsychotic used	Typical	92(44.9)	8(3.9)	84(41)
	Atypical	18(8.8)	1(0.5)	17(8.3)
	Antipsychotic with Antidepressant	69(33.7)	6(2.9)	63(30.7)
	Antipsychotic with mood stabilizer	26(12.7)	0(0)	26(12.7)
Blood TCHO	Normal	151(73.7)	7(3.4)	144(70.2)
	High	54(26.3)	8(3.9)	46(22.4)
Blood TG	Normal	167(81.5)	9(4.4)	158(77.1)
	High	38(18.5)	6(2.9)	32(15.6)

Factors associated with undiagnosed diabetes mellitus: In the bivariate analysis of variables with undiagnosed diabetes mellitus, sex, duration of antipsychotic treatment, total blood cholesterol and triglyceride were found to have a statistically significant association with the prevalence of undiagnosed DM.

However, in the multivariate logistic regression analysis of the study variables, there

was a statistically significant association only with sex and duration of antipsychotic treatment. Females were found to have 7.1 times to be at risk of having undiagnosed DM than males (AOR: 7.1, CI: 1.4 - 36.1), and as the duration of antipsychotic drug treatment increased by one year, the risk of having DM increased by 1.47 units (AOR: 1.47, CI: 1.021-2.125) (Table 4).

Table 3: Prevalence of undiagnosed diabetes mellitus by socio demographic characteristics of study participants at University of Gondar Hospital, northwest Ethiopia, 2016.

Variable	Category	UDM	
		Yes N (%)	No N(%)
Sex	Male	3 (1.5)	94(45.9)
	Female	12(5.9)	96(46.8)
Age	<25	0(0.0)	54(26.3)
	25-34	3(1.5)	71(34.6)
	35-45	5(2.4)	36(17.6)
	>45	7(3.4)	29(14.1)
Marital status	Married	4(2)	64(31.2)
	Single	7(3.4)	100(48.8)
	Divorced/separated	4(2)	25 (12.2)
	Widowed	0(0)	1(0.5)
Religion	Orthodox	12(5.9)	159(77.6)
	Muslim	2(1)	28(13.7)
	Others	1(0.5)	3(1.5)
Educational status	Illiterate	11(5.4)	90(43.9)
	Read and write	0(0.0)	39(19)
	1 ⁰ and 2 ⁰ school	3(1.5)	34(16.5)
	College and above	1(0.5)	27(13.2)
Residence	Rural	4(2)	77(37.6)
	Urban	11(5.4)	113(55.1)

Table 4: Multivariate and bivariate analysis of factors associated with undiagnosed diabetes mellitus among psychiatry patients taking antipsychotic drugs at the University of Gondar Hospital, northwest Ethiopia, 2016

Variable	Category	Undiagnosed DM		COR (95% CI)	AOR (95% CI)	P-value
		Yes N (%)	No N (%)			
Sex	Male	3(1.5)	94(45.9)	1		
	Female	12(5.9)	96(46.8)	3.91(1.07-14.32)*	7.1(1.436-35.4)	0.016**
BMI	Under	1(0.5)	18(8.8)	1		0.002
	Normal	1(0.5)	136(66.)	0.132(0.008- 2.2)	0.079(0.004-1.49)	0.091
	Overweight	11(5.4)	27(13.2)	7.33(0.87- 61.84)	7.1(0.68-74.51)	0.102
	Obese	2(1)	8(3.9)	4.5(0.355- 57.10)	2.18(0.133-36.06)	0.585
Duration	Years of drug use	-	-	1.44(1.157-1.80)*	1.47(1.021-2.12)**	0.038**
TCHO	Normal	7(3.4)	144(70)	1		
	High	8(3.9)	46(22.4)	3.57(1.23-10.40)*	0.22(0.036-1.408)	0.111
TG	Normal	9(3.4)	158(77)	1		
	High	6(2.9)	32(15.6)	3.29(1.09-9.895)*	1.65(0.403-6.83)	0.485

NB: *=Significant by bivariate analysis, **=significant by multivariate analysis

DISCUSSION

In this study, of 205 psychiatric patients, 15 (7.3%) met the WHO criteria for the DM. The prevalence of undiagnosed DM (7.3%) found in this study was higher than the estimated DM national prevalence of Ethiopia, 4.36% reported by the IDF in 2013 (3). This may be associated with poor health habits, low access to health care, the diabetogenic effect of the antipsychotic drugs and the global increase in the trend of the DM epidemic in developing countries.

The prevalence of undiagnosed DM among patients with psychiatric disorder in this study, (7.3%) (CI: 3.74 - 10.86), was lower than the findings of the studies among psychiatric patients in Palestine (10.8%) (14), Australia (12.1%) (15) and USA (10.2%) (16). It is likely that the differences observed in these studies were having a higher national prevalence of DM which could be due to lifestyle and genetic factors.

To the contrary, the prevalence (7.3%) of undiagnosed DM was also higher than the study finding in mental health care organizations in Holland, 6.5% (17), University of Rochester Medical Center London, 4.9% (18) and in Srilanka, 4.75% (19). This could be due to deficiency in DM screening and early diagnosis because of insufficient resources and practical considerations.

A higher prevalence of undiagnosed DM was observed in females (5.9%) than in males (1.5%), which is consistent with a study carried out on psychiatric patients in China (Male = 18.3% vs. Female = 31.3%) (20) and USA (Males = 9.5% vs. Females = 14.7%) (21). The possible reason for a highly represented undiagnosed DM among female psychiatric patients in this study was due to poor health seeking behavior and adopting a sedentary lifestyle.

Undiagnosed DM was significantly associated with duration of antipsychotic treatment in which as the duration of antipsychotic drug treatment increased by one year, the risk of having undiagnosed DM increased by 1.47 (AOR: 1.47, CI: 1.021-2.125). The finding of this study was also supported by a study done in South London, which showed an association of duration of antipsychotic treatment with an increased risk of DM (OR 1.01) (22). The

hypothesized diabetogenic effects of longer duration of antipsychotic treatment were on antipsychotic-induced weight gain. This starts with the eventual development of insulin resistance and pancreatic beta-cell failure (23).

Limitation of the study: Due to financial constraints, we were unable to incorporate tests like oral glucose tolerance test (OGTT). OGTT can increase the specificity of the study besides only the FPG test was used to evaluate undiagnosed DM this could underestimate the prevalence of undiagnosed DM. In addition, we used cross-sectional study design and this may not show exactly the cause and effect relationship between variables.

In conclusion, this study has found a higher prevalence of undiagnosed DM among psychiatry patients taking antipsychotics than the one in the general population of Ethiopia according to IDF 2014 estimated report. The risk factors associated with the prevalence of undiagnosed DM were the duration of antipsychotic drug treatment and sex of the participants.

We recommend early diagnosis and screening of DM in psychiatric patients, in particular, those patients with advanced age and longer duration of antipsychotic treatment. This will have a major importance to reduce the risk of DM-related complications like cardiovascular diseases by adopting lifestyle intervention.

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